REMARKS

The Present Invention

The present invention is directed to a method of inducing an immune response against at least one antigen in a mammal by inoculating the mammal with two different vectors encoding at least one antigen that is the same.

The Pending Claims

Claims 1-8, 21 and 22 are currently pending. All claims are directed to the methods.

The Amendments to the Specification and Claims

Page 1, line 3, of the specification has been amended to add the claim for priority. The claim for priority can be found on the original filing receipt and data transmittal sheet. Furthermore, page 5, line 7, of the specification has been amended to include a description for Figures 1, now labeled "Figures 1A-1E," in the "Description of the Drawings" as supported by the specification. The phrase "tumor growth" is supported at, for example, page 21, line 26, and the phrase "the mice were primed with various vectors 3 days post-intravenous challenge" is supported at, for example, page 21, line 31, to page 22, line 2. Furthermore, the phrase "array of vectors" has been replaced with "vectors," which can be found throughout the specification. Claims 1, 5, 21 and 22 have been amended to clarify that at least one antigen encoded on the first recombinant vector is also encoded on the second recombinant vector as a method for inducing an immune response against said antigen. Thus, no new matter has been added through amendment of the specification and claims.

The Office Action

Claims 1-8, 21 and 22 have been rejected under 35 U.S.C. § 112, first and second paragraphs, and claims 1-3 and 5-7 have been rejected under 35 U.S.C. § 103. Reconsideration of these rejections is hereby requested.

Discussion of Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-8, 21 and 22 have been rejected under Section 112, first paragraph, as allegedly not enabled for obtaining an immune response using any combination of vectors as claimed, or inducing a therapeutic or prophylactic immune response against an antigen using the claimed invention. Applicants traverse this rejection for the reasons set forth below.

Applicants respectfully submit that the specification teaches how to make and use the claimed methods. For example, at page 10, lines 14-30, the specification teaches how to

construct and use vaccinia virus vectors for the claimed methods. The specification recites vector specific cloning sites for inserting a gene encoding an antigen associated with a disease, as well as methods of introducing a recombinant vector into a mammal to induce an immune response to such antigens, for example, at page 17, lines 10-27. In sum, the specification teaches how to construct recombinant viral vectors encoding disease-associated antigens, which are known in the art. The specification further teaches how to use these recombinant vectors for inducing an immune response in mammals. Therefore, the specification provides enabling disclosure for the claimed methods.

While Wang et al. does not teach the claimed methods, Wang et al. provides support for Applicant's use of β-gal as a disease-antigen model system to teach how to make and use the present invention. Furthermore, Neeley et al. (*The Prostate*, 53:183-191 (2002), copy enclosed) also uses β-gal as a model system for mimicking the immune response to disease-associated antigens. Neeley et al. is a later-published scientific work that demonstrates that an ordinarily skilled artisan correlates a therapeutic or prophylactic immune response against β-gal with a therapeutic or prophylactic immune response against a disease-associated antigen. Therefore, Neeley et al. provides further support for Applicants' use of the β-gal model system in enabling the claimed invention.

The Office also alleges that the claimed methods cover gene therapy. This contention is not supported by the claims whether viewed alone or in light of the specification. The phrase "gene therapy" is never even recited in the instant application. Furthermore, the targeting of specific tissues is not required to practice the claimed methods, as is the case for gene therapy. Also, unlike gene therapy, sustained expression of exogenous DNA is not required to practice the instant invention. Thus, Applicants respectfully submit that the Office's reliance on gene therapy in support of an enablement rejection of the pending claims is misplaced and inappropriate. Given that the instantly claimed invention is not directed to gene therapy, there is no basis for the Office to contend that the relevant art is unpredictable.

Next, the Office alleges that the specification does not provide adequate guidance for treatment, since β-gal is a foreign protein, and other disease-related antigens are self-proteins, and thus, β-gal and disease-related antigens differ in their ability to induce an immune response. Specifically, the Office contends that the specification does not provide any guidance to treat cancer using MART-1, gp100, TRP-1, or TRP-2, since there is no correlation between the epitopes of these antigens and those of β-gal.

First, for the reasons set forth above, β-gal is an appropriate model system to mimic the immune response to other antigens. Second, the treatment of cancer per se is not claimed; rather, what is claimed is a method of inducing an immune response to a disease-associated

antigen, such as an antigen associated with the disease cancer. Third, Applicants direct the Office's attention to Dudley et al. (*Science*, 298: 850-854 (2002), copy enclosed). Dudley et al. demonstrates the efficacy resulting from the use of MART-1 for directing an immune response to cancerous cells. Furthermore, Dudley et al. indicates that there is overwhelming evidence that lymphocytes are immuno-targeted to cancerous cells relative to normal cells, due to over-expression of disease-associated antigens on cancerous cells. The instant specification teaches how to make and use the claimed invention commensurate with the scope of the claims, as evidenced by the aforementioned, later-published articles. There is sufficient teaching in the specification to induce an immune response against a disease-associated antigen as claimed.

In view of the foregoing, Applicants submit that claims 1-8, 21 and 22 are enabled. Accordingly, Applicants request the withdrawal of this rejection.

Discussion of Rejection under 35 U.S.C. § 112, second paragraph

Claims 1-8, 21 and 22 have been rejected under Section 112, second paragraph, as allegedly indefinite for failing to point out particularly and claim distinctly the subject matter of the invention. Applicants respectfully disagree with this rejection. In order to expedite prosecution of this application and not in acquiescence of the rejection, however, Applicants have amended claims 1, 5, 21 and 22. Amended claims 1, 5, 21 and 22 clarify that at least one antigen encoded by the second recombinant vector is the same as at least one of the previously inoculated antigens encoded by the first recombinant vector. Furthermore, claim 1 has been amended to clarify that the induced immune response is directed towards antigens, which are the same and which are encoded on the first and second recombinant vectors.

In view of the foregoing, Applicants submit that claims 1-8, 21 and 22 are definite. Accordingly, Applicants respectfully request withdrawal of the rejection under Section 112, second paragraph.

Discussion of Rejection under 35 U.S.C. § 103

Claims 1-3 and 5-7 remain rejected under Section 103(a) as allegedly obvious in view of and, therefore, unpatentable over Wang et al. (J. Immunol., (1995 May 1) 154 (9): 4685-92). This rejection is traversed for the reasons set forth below.

Applicants respectfully submit that claims 1-3 and 5-7 are not obvious in view of Wang et al. since the pre-immunization experiment on page 4689 and Figure 4 of Wang et al. do not teach inducing an immunological response by inoculating with different vectors encoding the same antigen, as does the present invention. The Office admits as much on page 9 of the instant Office Action. The Office, however, alleges that the present invention would be obvious to one

of ordinary skill in the art in view of Wang et al. Furthermore, the Office claims that the standard for obviousness merely requires that one of ordinary skill in the art at the time the invention was made would have been motivated to modify the teachings in the art to make and use the claimed invention, but the prior art need not specifically suggest or teach such a modification. This standard is not the appropriate standard to determine obviousness, since the level of skill in the art must be qualified to provide the motivation to modify or combine the prior art to reach the claimed invention. *See Al-Site Corp. v. VSI Int'l Inc.*, 174 F.3d 1308 (Fed. Cir. 1999). In order to use the knowledge of the skilled artisan as the motivating factor to modify the prior art, the Office must make a factual finding as to the specific understanding within the knowledge of the skilled artisan that would have provided the motivation to modify the prior art, thereby rendering the claimed invention obvious. *See In re* Kotzab, 217 F.3d 1365 (Fed. Cir. 2000). The Office has not made such a finding.

The appropriate test to establish a *prima facie* case of obviousness demands that the Office satisfy three requirements: (1) the Office must identify some suggestion or motivation, either in the references relied upon or in the knowledge generally available in the art, to modify the references in such a way as to arrive at the invention claimed, (2) there must be a reasonable expectation of success, and (3) the prior art references relied upon must teach or suggest all of the elements of the claim. As stated above, the Office has not met this burden by simply asserting that it believes that one of ordinary skill in the art would have found the present invention obvious.

None of the cited references disclose the claimed methods of inducing an immune response. As pointed out above, and admitted by the Office, Wang et al. does not disclose pre-immunization with a vector encoding an antigen, followed by immunization with a different vector encoding the same antigen. Wang et al. requires pre-immunization with a wild-type viral vector, and neither Wang et al. nor the art, itself, provides any incentive to deviate from this teaching. Thus, the Office cannot rely on Wang et al. to establish *prima facie* obviousness. First, Wang et al. does not suggest or motivate one to modify the art to arrive at the claimed invention. It is not enough for the Office to assert that one ordinarily skilled in the art would have been motivated to modify the reference; some greater showing of motivation is necessary to establish a *prima facie* case for obviousness. Second, there is no basis in Wang et al. to establish a reasonable likelihood of success for the claimed invention. Finally, not all limitations of the present invention are recited in the prior art. Moreover, the Office has not cited any other reference to cure the deficiencies of Wang et al., whether taken separately or together.

Also, in response to the Office's assertion that Applicants have not argued the unobviousness of claim 5 in light of the fact that each viral vector encodes viral proteins,

Applicants point out that the two different viral vectors express two different foreign proteins upon each immunization. The present invention calls for the immunization of at least one common antigen.

Claims 1-3 and 5-7 have been rejected under Section 103(a) as allegedly obvious in view of and, therefore, unpatentable over Wang et al. in view of Zhai et al. (Jan. 15, 1996, J. Immunol., Vol. 156, No. 2, pages 700-710). Applicants traverse this rejection for the reasons set forth below.

Wang et al. does not teach or suggest the subject matter of claims 1-3 and 5-7 for the reasons set forth above. Zhai et al. does not cure the deficiencies of Wang et al. Zhai et al. is directed towards administering an adenoviral vector encoding β-gal. Zhai et al. does not teach, let alone suggest, inoculating a mammal with a vector encoding at least one antigen followed by inoculating the mammal with a different vector encoding at least one antigen that is the same in order to induce an immune response, as does the present invention. Again, the Office merely makes a broad assertion that it would have been obvious to one of ordinary skill in the art to make the claimed invention even though there is no suggestion or motivation in the prior art to do so. As stated above, based on the appropriate test for determining obviousness, the Office has not made a finding as to the specific understanding within the knowledge of the ordinarily skilled artisan that would have provided the motivation to modify the prior art, and thus, has not met its burden. Accordingly, this rejection cannot stand.

Conclusion

The application is considered to be in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

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